

REMARKS

Claims 1, 4-17 and 38-40 are pending. Claim 1 is amended and claims 2, 3, and 18-37 are canceled.

Examiner Interview

On June 23, 2010, Examiners Shirley Gembeh and Robert Hayes had a telephonic interview with inventor attorneys for Applicants, Janet S. Hendrickson and John Roedel. The Examiners and the Applicants' representatives discussed the outstanding rejections. In particular, Examiner Hayes suggested claim amendments similar to those made herein and indicated these amendments would advance prosecution. However, no agreement was reached regarding the 35 U.S.C. § 103 or obviousness-type double patenting rejections. Therefore, applicants have expanded these arguments in the response below.

35 U.S.C. § 103 rejection

Reconsideration is respectfully requested of the rejection of claims 1, 4-19 as unpatentable over Campbell (US 6,265,386) in view of Pusztai et al. (US 6,110,891) under 35 U.S.C. § 103. Claim 1 is directed to a method for reducing oral mucositis in a human or animal cancer patient undergoing radiation therapy. The method comprises administering to the cancer patient undergoing radiation therapy in need of reduction of oral mucositis an effective amount of a protective agent selected from the group consisting of D-methionine, L-methionine, a mixture of D-methionine and L-methionine, and a pharmaceutically acceptable salt thereof.

The Campbell '386 reference describes methods for reducing hearing or balance loss, damage to ear cell, weight loss, gastrointestinal toxicity, neurotoxicity, alopecia, and for prolonging survival in patients undergoing treatment with anti-tumor platinum coordination compounds, loop diuretics, aminoglycoside antibiotics, iron chelating agents, quinine, quinidine, or those exposed to toxic levels of noise or radiation. These methods comprise administering an effective amount of a methionine protective agent. The Campbell '386 patent does not disclose the administration of D-methionine, L-methionine, or D,L-methionine to a cancer patient undergoing radiation therapy in need of reduction of oral mucositis. Pusztai teaches treating mucosal cell damage by administering lectins.

Further, there can be no basis for obviousness where the prior art further fails to recognize the potential effect of the treating agent against the condition specified in the claim. As the C.C.P.A. has stated in reversing an obviousness rejection of a claim to a method of treating a specified condition with a defined treatment agent based on the inherent effect of treating a different condition with a similar agent.

[Inherency] is quite immaterial if, as the record establishes here, one of ordinary skill in the art would not appreciate or recognize that inherent result, *in re Shetty*.¹

The method claims at issue in *Shetty* were directed to methods for appetite control and the cited prior art disclosed compounds and dosages useful for combating microbial infestation. The *Shetty* court stated that the Office had "failed to show a reasonable expectation, or some predictability" that the prior art compound disclosed in the first reference would be an effective appetite suppressant if administered in the dosage disclosed in the second reference and that the Office's hindsight assertion that the dosages would make the weight loss method obvious was insufficient.² Similar to *Shetty*, claim 1 recites a method wherein methionine is administered to a cancer patient undergoing radiation therapy in need of reduction of oral mucositis.

Since oral mucositis does not necessarily and inevitably arise from radiation therapy of a cancer patient, claim 1 cannot be obvious over Campbell in view of Pusztai. Novelty over Campbell is established because administering methionine to a cancer patient undergoing radiation therapy in need of reduction of oral mucositis is not inherent in Campbell. Non-obviousness over Campbell is established because: (i) a person of ordinary skill in the art would not read Campbell as dealing with oral mucositis; and (ii) nothing in Campbell provides a basis for predicting the efficacy of methionine in reducing oral mucositis in cancer patients undergoing radiation therapy in need of such reduction.

While the Office asserts and the Malone declaration discusses that oral mucositis is sometimes broadly classified as a form of gastrointestinal toxicity, oral mucositis is an effect distinctly separate from the effects ordinarily contemplated by "gastrointestinal toxicity" such as nausea, diarrhea and abdominal pain, and generally results from different pathological mechanisms. Claim 1 is directed to the species of "oral mucositis" and this species of gastrointestinal mucositis is not explicitly or implicitly disclosed by the Campbell '386 patent. A

¹ 195 U.S.P.Q. 753.

² See *id.* at 756.

person of ordinary skill in the art would not read Campbell as dealing with oral mucositis. Campbell would not have led one skilled in the art to try administration of methionine to reduce oral mucositis; and, even if one were to try, Campbell would not have provided a basis for predicting the efficacy of methionine for reducing oral mucositis.

The Office action focuses on the Campbell observation that "exposure to radiation, whether intentional as in radiation therapy, can result in gastrointestinal disorders." But the Office cites no evidence that one skilled in the art would read Campbell's reference to gastrointestinal disorders including stomatitis as relating to oral mucositis. Although oral mucositis is sometimes classified within the ambit of "gastrointestinal disorders," and can also be one of multiple species within the generic term stomatitis, a person skilled in the art would not have contemplated any symptoms arising from radiation other than the conventional "gastrointestinal" symptoms of nausea, diarrhea and abdominal pain upon review of the Campbell reference. Campbell also would not have suggested dealing with the local effects of otolaryngeal radiation, the main radiation treatment by which oral mucositis can be induced.

Pusztai is cited as teaching that gastrointestinal disorders resulting from the administration of radiation may include the mouth. But there is still no evidence that Campbell was addressing oral mucositis, or that one skilled in the art would have read Campbell that way. Moreover, Pusztai fails to suggest that administration of methionine is effective against any form of cancer. On the contrary, Pusztai generally discusses treatment of mucositis only by administration of lectins. Although the lectin-rich diets administered by Pusztai incidentally contain methionine, Pusztai does not anticipate the instant claims because the amount of L-methionine administered in the diet of the subjects was only 0.1%-0.2% of the total composition. Further, a person skilled in the art would have expected that L-methionine, a naturally occurring amino acid, would be present in a food composition and that it would perhaps serve other nutritive needs of the cancer patient. But there is absolutely nothing in Pusztai suggesting that the methionine component of the diet has any ameliorative effect on any cancer symptom, or on any side effect caused by cancer therapy, whether radiation or otherwise. Thus, Pusztai would not have led a skilled person to contemplate that methionine alone would provide a therapeutic benefit to cancer patients undergoing radiation therapy and in need of reduction of oral mucositis. Much less can any suggestion be found in Pusztai for treatment of the specific condition of oral mucositis by administration of methionine.

Thus, Pusztai does not compensate for the deficiencies of Campbell in failing to teach or suggest the administration of methionine to reduce oral mucositis.

In sum, the pending claims are patentable over the cited references.

Obviousness-type double patenting rejections

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.³ However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.⁴

Reconsideration is respectfully requested of the rejection of claims 1, 4-19, and 38-40 over claims 1-9, 11-13, 15-25, and 27-33 of U.S. Application No. 10/694,432. U.S. Application No. 10/694,432 is abandoned.

Reconsideration is respectfully requested of the rejection of claims 1, 4-19, and 38-40 over claims 1-29 of U.S. Patent No. 7,557,142 as being unpatentable under the doctrine of obviousness-type double patenting. The '142 patent contains claims directed to methods for reducing ototoxicity in a patient in need thereof undergoing treatment with an anti-tumor platinum-coordination compound by administering L-methionine or a mixture of D- and L-methionine. The '142 patent does not claim methods wherein methionine is administered to cancer patients undergoing radiation therapy in need of reduction of oral mucositis. The claims of the '142 patent are not directed to reducing oral mucositis in a cancer patient undergoing radiation therapy, the claims do not include all the elements of subject claims 1, 4-19, and 38-40. Further, as discussed above in connection with *in re Shetty*, in order to be obvious, the Office must show there would have been some reasonable expectation that administering methionine would have been effective for reducing oral mucositis in such a patient. There would have been no reason to expect that a patient undergoing treatment with an anti-tumor platinum-coordination compound as described in the '142 patent would have necessarily experienced oral mucositis and even if the patient did experience oral mucositis, the Office has provided no reasonable

³ *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991).

⁴ *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

expectation of success that administration of methionine would have reduced oral mucositis in cancer patients undergoing radiation therapy in need of such reduction.

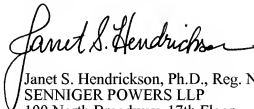
Reconsideration is respectfully requested of the rejection of claims 1, 4-19, and 38-40 over claims 1-36 of U.S. Patent No. 6,187,817. Claims 1-28 of the '817 patent are directed to a method for preventing or reducing ototoxicity, claims 29-30 are directed to methods of preventing or reducing weight loss, claims 31-32 are directed to methods of preventing or reducing gastrointestinal toxicity, claims 33-34 are directed to methods of preventing or reducing neurotoxicity, and claims 35-36 are directed to methods of preventing or reducing alopecia wherein all of these conditions arise from treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound. Accordingly, because the claims of the '817 patent are not directed to administering methionine to a cancer patient undergoing radiation therapy in need of reduction of oral mucositis, the claims do not include all the elements of subject claims 1, 4-19, and 38-40. Further, as discussed above in connection with *in re Shetty*, in order to be obvious, the Office must show there would have been some reasonable expectation that methionine would have been effective for reducing oral mucositis in such a patient. There would have been no reason to expect that a patient undergoing treatment with an anti-tumor platinum-coordination compound as described in the '817 patent would have necessarily experienced oral mucositis and even if the patient did experience oral mucositis, the Office has provided no reasonable expectation of success that administration of methionine would have reduced oral mucositis in cancer patients undergoing radiation therapy in need of such reduction.

CONCLUSION

Applicant submits that the present application is now in a condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,

A handwritten signature in black ink, reading "Janet S. Hendrickson", with a stylized flourish at the end.

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